(1) Claims 39-44, 47, 48, 50, and 51 were rejected under 35 USC § 112, second paragraph as "indefinite" in their recitation of the phrase "extracellular domain." Claims 47 and 48 have been canceled. The remaining claims no longer recite the phrase "extracellular domain," therefore, the present rejection is believed to be moot.

(2) Claims 39-44 and 46-51 have been rejected under 35 USC §112, first paragraph for alleged lack of enablement. The Examiner noted that claims failed to contain any functional limitation, and suggested that "enablement is limited to those structural variants [of the polypeptide of SEQ ID NO: 39] which inhibit VEGF-stimulated epithelial cell growth.

Claims 47 and 48 have been canceled, which moots their rejection. As discussed below, Applicants rely on the ability of the claimed polypeptides to function as viral receptors. This activity is now recited in the claims, providing a functional limitation.

The present application, and its earliest priority application 60/062,826 filed on October 24, 1997, disclosed that the PRO246 polypeptide shares significant homology to the human Coxsackie-adenovirus receptor. The disclosure further states that a portion of the PRO246 polypeptide has a significant homology with the human cell surface protein HCAR. Considering its significant homology to the human Coxsackie adenovirus receptor, applicants further suggest the PRO246 polypeptide to be a novel cell surface virus receptor.

It was known in the art at the earliest priority date of the present application that HCAR is a human cellular receptor for the group B Cocksackie-viruses (CVB), and human subgroup C adenoviruses (Ad2 and Ad5) (see Tomko *et al., Proc. Natl. Acad. Sci. USA* 94:3352-3356 (April 1997), a copy of which is submitted with the attached Information Disclosure Statement). It was also well known that the Coxsackie-virus is involved in a variety of diseases, most prominently, human myocarditis, cardiomyopathy, meningoencephalitis, and acute pancreatis (see, e.g. column 2, lines 3-6 of US 5,942,606 of record). In addition, virus assays were well known in the art at the earliest priority

date of the present application, as demonstrated. for example, by the disclosure of Tomko *et al., supra*, and also by Example X of US 5,942,606. Such assays could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor. Consequently, based on general knowledge in the art and the disclosure of the present application, at the earliest priority date of the present application one was able to make and use the claimed invention, without undue experimentation. It is well established that the fact that some experimentation may be necessary, or time consuming, does not make such experimentation "undue," as long as the techniques used are readily available and routine, as they are in the present case. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(3) Claims 39-44, 50, and 51 were rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention."

The cancellation of claims 47 and 48 moots their rejection. The rejection of the remaining claims is respectfully traversed. As discussed above, the claimed polypeptides are characterized to function as viral receptors. Based upon the high degree of homology of the PRO246 polypeptide to a known viral receptor, general knowledge in the art as of the earliest priority date of the present application, as well as the disclosure of the present application, one skilled in the art at the earliest priority date would have reasonably concluded that Applicants were in the possession of the invention claimed. Accordingly, the Examiner is respectfully requested to withdraw the present rejection.

The foregoing arguments are further supported by the issuance of US 5,942,606, disclosing a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application. The disclosure of US 5,942,606 is very similar to the disclosure of the present application, and is devoid of any experimental data

demonstrating the antiviral activity of ACVRP, or identifying the specific viruses associated with this receptor. The issuance of the presumptively valid US 5,942,606 is *prima facie* evidence that such experimental data are not required to comply with the requirements of patentability, including the enablement and written description requirements. The same standard should be applied in the present case, which claims the priority of October 24, 1997, preceding the earliest priority date (November 24, 1997) of US 5,942,606. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection

Claim Rejections - 35 USC §102

Claims 39046, 49, and 50 were rejected under 35 USC § 102(e2) "as being anticipated by Lal et al. 5,942,606."

As discussed above, the present application is entitled to the priority date of October 24, 1997, which precedes, by one month, the earliest priority date of Lal et al. (November 24, 1997). Accordingly Lal et al. is not prior art against the present application, and the present rejection should be withdrawn.

Applicants note the additional art cited but not relied upon, none of which is believed to anticipate or render obvious the claims pending.

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding, she is invited to contact the undersigned attorney at the telephone number shown below.

It is emphasized that all amendments made herein are without prejudice, and without acquiescing to any of the rejections raised in the Office Action of October 2, 2002, or any reasoning underlying the rejections. The sole purpose of the present rejections is to facilitate the prosecution of the present application. Applicants specifically retain the right the pursue any subject matter not literally covered by the current claims in any or more continuing applications.

Attached to the present Amendment and Response is a marked up copy of the amended claims entitled "**Version with markings to show changes made.**"

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 08-1641 (Docket No.: 39780-1618P2C21). A duplicate copy of this paper is enclosed.

Respectfully submitted,

Date: February 19, 2003

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Version with Markings to Show Changes Made

In the Claims:

Claims 47 and 48 have been canceled, without prejudice.

Claims 39-44 have been amended as follows:

39. (Once amended) An isolated polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396,

wherein said polypeptide is a viral receptor.

40. (Once amended) The isolated polypeptide of claim 39 having at least 85% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396.

41. (Once amended) The isolated polypeptide of claim 39 having at least 90% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396.

42. (Once amended) The isolated polypeptide of claim 39 having at least 95% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396.

43. (Once amended) The isolated polypeptide of claim 39 having at least 99% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396.

44. (Once amended) An isolated polypeptide comprising:

(a) the amino acid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(b) the aminoa cid sequence of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;

[(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 17 (SEQ ID NO: 39), lacking its associated signal peptide;] or

[(e)] (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209396.